=> d ibib abs 1-9

L17 ANSWER 1 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 2000:608377 SCISEARCH

THE GENUINE ARTICLE: 340WT

TITLE: Leptin contributes to the protection of human leukemic

cells from cisplatinum cytoxicity

AUTHOR: Efferth T (Reprint); Fabry U; Osieka R

CORPORATE SOURCE: UNIV ERLANGEN NURNBERG, INST CLIN & MOL VIROL,

SCHLOSSGARTEN 4, D-91054 ERLANGEN, GERMANY (Reprint); RHEIN WESTFAL TH AACHEN, HOSP INTERNAL MED 4, D-52057

AACHEN, GERMANY

COUNTRY OF AUTHOR:

GERMANY

SOURCE:

ANTICANCER RESEARCH, (JUL-AUG 2000) Vol. 20, No.

4, pp. 2541-2546.

Publisher: INT INST ANTICANCER RESEARCH, EDITORIAL OFFICE 1ST KM KAPANDNTIOU-KALAMOU RD KAPANDRITI, POB 22, ATHENS

19014, GREECE.
ISSN: 0250-7005.

DOCUMENT TYPE:

Article; Journal

FILE SEGMENT: LANGUAGE: LIFE English

REFERENCE COUNT:

25

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Leptin (ob gene) and its cognate receptor (obr) are relevant for fat metabolism. Obr shares homology with the IL-

6 signal transducer gp130 and is expressed in hematopoietic cells. Since cytokines and growth factors regulate both hematopoiesis and response to chemotherapy, we tested the hypothesis of whether leptin protects leukemic cells from cytotoxicity of cisplatinum. Antisense phosphorothicate oligodeoxynucleotides (ODNs) and antisense peptide nucleic acids (PNAs) complementary to the obr gene were first tested for their growth inhibitory activity in obr expressing leukemic cells. Liposome-mediated transfection of ODNs (1-2 mu M) or PNAs (0.01-1 mu M) inhibited growth up to 50%. Combination treatments of

cisplatinum and 0.01 mu M PNA reduced growth more than cisplatinum alone. Vice versa, recombinant human leptin (rhL) diminished cisplatinum-induced growth inhibition. Finally, we investigated whether rhL affects cisplatinum-induced DNA damage and repair in the housekeeping gene beta-actin by means of real time TaqMan(R) polymerase chain reaction. RhL reduced DNA damage and increased DNA repair. The effects are, however,

modest and **leptin** is probably not the only player in the armory of growth factors which affect drug resistance.

L17 ANSWER 2 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 1999:153417 SCISEARCH

THE GENUINE ARTICLE: 166UL

THE GENOTIVE ARTICLE. 1000

TITLE: Phenotypic abnormalities in macrophages from

leptin-deficient, obese mice

AUTHOR: Lee F Y J; Li Y B; Yang E K; Yang S Q; Lin H Z; Trush M A;

Dannenberg A J; Diehl A M (Reprint)

CORPORATE SOURCE: JOHNS HOPKINS UNIV, SCH MED, DEPT MED, 912 ROSS BLDG, 720

RUTLAND ST, BALTIMORE, MD 21205 (Reprint); JOHNS HOPKINS UNIV, SCH MED, DEPT MED, BALTIMORE, MD 21205; JOHNS HOPKINS UNIV, DEPT ENVIRONM HLTH, BALTIMORE, MD 21205; CORNELL UNIV, COLL MED, DEPT MED, NEW YORK, NY 10021;

STRANG CANC PREVENT CTR, NEW YORK, NY 10021

COUNTRY OF AUTHOR: US

SOURCE: AMI

AMERICAN JOURNAL OF PHYSIOLOGY-CELL PHYSIOLOGY, (FEB

1999) Vol. 45, No. 2, pp. C386-C394.

Publisher: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE,

BETHESDA, MD 20814.

ISSN: 0363-6143.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE LANGUAGE: English

REFERENCE COUNT: 45

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Obesity is a complex syndrome that involves defective signaling by a number of different factors that regulate appetite and energy homeostasis. Treatment with exogenous leptin reverses hyperphagia and obesity in ob/ob mice, which have a mutation that causes leptin deficiency, proving the importance of this factor and its receptors in the obesity syndrome. Cells with leptin receptors have been identified outside of the appetite regulatory centers in the brain. Thus leptin has peripheral targets. Because macrophages express signaling-competent leptin receptors, these cells may be altered during chronic leptin deficiency. Consistent with this concept, the present study identifies several phenotypic abnormalities in macrophages from ob/ob mice, including decreased steady-state levels of uncoupling protein-2 mRNA, increased mitochondrial production of superoxide and hydrogen peroxide, constitutive activation of CCAAT enhancer binding protein (C/EBP)-beta, an oxidant-sensitive transcription factor, increased expression of interleukin-6 and cyclooxygenase (COX)-2, two C/EBP-beta target genes, and increased COX-2-dependent production of PGE(2). Given the importance of macrophages in the general regulation of inflammation and immunity, these alterations in macrophage function may contribute to obesity-related pathophysiology.

L17 ANSWER 3 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 97:888491 SCISEARCH

THE GENUINE ARTICLE: YG935

TITLE: Transforming growth factor-beta enhances and

pro-inflammatory cytokines inhibit OB gene expression in

3T3-L1 adipocytes

AUTHOR: Granowitz E V (Reprint)

CORPORATE SOURCE: BAYSTATE MED CTR, DEPT MED, DIV INFECT DIS, SPRINGFIELD,

MA 01199 (Reprint); TUFTS UNIV, SCH MED, SPRINGFIELD, MA

01199 USA

COUNTRY OF AUTHOR:

SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (

17 NOV 1997) Vol. 240, No. 2, pp. 382-385.

Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS, 525

B ST, STE 1900, SAN DIEGO, CA 92101-4495.

ISSN: 0006-291X. Article; Journal

DOCUMENT TYPE: Article; FILE SEGMENT: LIFE

LANGUAGE: English
REFERENCE COUNT: 40

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

Leptin is a protein which is encoded by the obese

(ob) gene. It is synthesized by adipocytes and binds to receptors in the hypothalamus, thereby suppressing appetite and increasing the metabolic rate. When mouse 3T3-L1 cells are induced to differentiate into adipocytes, they bean to constitutively express low levels of oh mRNA. Using reverse transcription and a semi-quantitative polymerase chain reaction, the experiments described herein demonstrate that the antiinflammatory cytokine transforming growth factor-p increases steady state ob mRNA. Conversely, treatment of 3T3-L1. adipocytes with the pro-inflammatory cytokines interleukin-1 beta, interleukin-6, interleukin-11, and tumor necrosis factor-alpha results in a decrease in ob transcripts. When considered in the context of animal studies showing that interleukin-1 and tumor necrosis factor-alpha induce

leptin and ob mRNA, these results suggest that pro-inflammatory
cytokines induce ob gene transcription in vivo via secondary mediators
such as transforming growth factor-beta. (C) 1997 Academic Press.

L17 ANSWER 4 OF 9

PCTFULL COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER:

2000007014 PCTFULL ED 20020515 LEPTIN-MEDIATED GENE-INDUCTION

TITLE (ENGLISH): TITLE (FRENCH):

INDUCTION DE GENES A MEDIATION PAR LA LEPTINE

INVENTOR(S):
BROEKAERT, Daniel;

VANDEKERCKHOVE, Joel, Stefaan;

VERHEE, Annick; WAELPUT, Wim; TAVERNIER, Jan

PATENT ASSIGNEE(S):

VLAAMS INTERUNIVERSITAIR INSTITUUT VOOR BIOTECHNOLOGIE

VZW:

BROEKAERT, Daniel;

VANDEKERCKHOVE, Joel, Stefaan;

VERHEE, Annick; WAELPUT, Wim; TAVERNIER, Jan

LANGUAGE OF PUBL.:

English Patent

DOCUMENT TYPE: PATENT INFORMATION:

NUMBER KIND DATE

WO 2000007014

A2 20000210

DESIGNATED STATES

W:

AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD

TG

APPLICATION INFO.: PRIORITY INFO.:

WO 1999-EP5489

A 19990727

EP 1998-98202524.9

19980728

ABEN Using the PC12 cell line as a model system a series of transcripts induced through activation

of the leptin receptor or gpl30 was identified. Based on kinetic studies on undifferentiated PC12

cells, two distinct gene-sets could be discerned: STAT-3, SOCS-3, Metallothionein-II, the

serine/threonine kinase Fnk and the rat homologue of MRF-1 which are immediate early response genes,

and Pancreatitis Associated Protein I, Squalene Epoxidase,

Uridinediphosphate Glucuronyl Transferase

and Annexin VIII, which are late induced target genes. In the latter case only, a strong

co-stimulation with the adenylate cyclase activator forskolin was observed. Two additional $\,$

transcripts encoding Leptin Induced Protein I (LIP-I) and Leptin Induced Protein II (LIP-II) were

also identified. LIP-II is a rat orthologue of the human Down Syndrome Cell Adhesion Molecule

(DS-CAM). In both cases, no forskolin co-stimulatory effect was observed. On PC12 cells

differentiated to a neural phenotype by combined β-NGF and forskolin treatment, Pancreatitis

Associated Protein III, Peripherin and Mx2 protein were further identified as being regulated by

leptin. Finally, from an RDA experiment using mRNA from either hyper-

IL-6- or leptin-induced PC12 cells, the Reg gene, another member of the Pancreatitis Associated Protein family, and HIP-1 were identified as selectively up-regulated by H-IL-6. STAT-3 and SOCS-3 have been recognized in leptin signalling i(in vivo) before. In this invention it is also demonstrated that leptin modulates the i(in vivo) expression of the MT-II, Fnk and Pancreatitis Associated Protein I genes. L'utilisation de la lignee cellulaire PC12 en tant que systeme modele a permis d'identifier une serie de transcrits induits par l'activation du recepteur de la leptine ou gp130. A partir d'etudes cinetiques de cellules PC12 indifferenciees, deux ensembles distincts de genes ont pu etre distingues: STAT-3, SOC-3, metallothioneine-II, serine/threonine kinase Fnk et homologue murin de MRF-1, genes de la reponse precoce immediate d'une part, Proteine associee a la pancreatite I, Squalene Epoxidase, Uridinediphosphate Glucuronyl Transferase et Annexine VIII, genes cibles a induction tardive d'autre part. Dans le dernier cas seulement, on a pu observer une forte co-stimulation par la forskoline, un activateur de l'adenylate cyclase. Deux autres transcrits codant pour la proteine induite par la leptine I (LIP-1) et pour la proteine induite par la leptine II (LIP-II) ont egalement ete observes. LIP-II est un hortologue murin de la molecule d'adhesion cellulaire du syndrome de Down d'origine humaine (DS-CAM). Dans les deux cas, aucun effet co-stimulateur de la forskoline n'a ete observe. Sur des cellules PC12 differenciees en phenotype neuronal par un traitement combine β -NGF/forskoline, on a constate par ailleurs que la proteine III associee a la pancreatite, la peripherine et la proteine Mx2 etaient regulees par la leptine. Enfin, a partir d'une experience de ration dietetique recommandee faisant intervenir de l'ARN m provenant de cellules PC12 induites par hyper-IL-6 ou par la leptine, on a constate une regulation positive du gene Reg, autre membre de la famille des proteines associees a la pancreatite, et de HIP-1 par H-IL-6. STAT-3 et SOCS-3 avaient ete observes auparavant i(in vivo) dans la signalisation de la leptine. Cette invention demontre egalement que la leptine module l'expression i(in vivo) des genes MT-II, Fnk et de la proteine I associee a la pancreatite. ANSWER 5 OF 9 COPYRIGHT 2004 Univentio on STN PCTFULL ACCESSION NUMBER: 1999053927 PCTFULL ED 20020515 TITLE (ENGLISH): METHODS FOR TREATING AND PREVENTING INSULIN RESISTANCE AND RELATED DISORDERS TITLE (FRENCH): PROCEDES POUR TRAITER ET PREVENIR LA RESISTANCE A L'INSULINE ET LES TROUBLES QUI Y SONT LIES INVENTOR(S): GREENBERG, Andrew, S. TRUSTEES OF TUFTS COLLEGE; PATENT ASSIGNEE(S): GREENBERG, Andrew, S. LANGUAGE OF PUBL.: English

KIND

DATE

Page 4

DOCUMENT TYPE:

PATENT INFORMATION:

Patent

NUMBER

L17

ABFR

WO 9953927 A1 19991028

DESIGNATED STATES

W:

JP US AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL

PT SE

APPLICATION INFO.: PRIORITY INFO.:

WO 1999-US8364

A 19990416

US 1998-60/082,152 19980417 US 1998-60/082,741 19980423

ABEN The invention provides methods, therapeutics and kits for treating and preventing diseases or

conditions associated with excessive lipolysis, in particular

TNF-α induced lipolysis, and/or

excessive free fatty acid levels. Exemplary conditions include

insulin-resistance, diabetes, in

particular NIDDM, obesity, glucose intolerance, hyperinsulinemia,

polycystic ovary syndrome, and

coronary artery disease. In a preferred embodiment, the method includes administering to a subject

in need a pharmaceutically effective amount of an inhibitor of the JNK

signal transduction pathway and/or an inhibitor of the MAPK/ERK signal transduction pathway and/or a

stimulator of the p38

signal transduction pathway.

ABFR L'invention concerne des procedes, des moyens therapeutiques et des kits destines au traitement

et a la prevention des maladies et etats associes a une lipolyse excessive, en particulier a la

lipolyse induite par TNF-α, et/ou a des concentrations excessives d'acides gras libres. En

guise d'exemple, on cite la resistance a l'insuline, le diabete (en particulier le diabete non

insulinodependant), l'obesite, l'intolerance au glucose,

l'hyperinsulinemie, le syndrome de

Stein-Leventhal-Cohen et la coronaropathie. Dans un mode de realisation prefere, le procede consiste

a administrer a un sujet souffrant une quantite pharmaceutiquement efficace d'un inhibiteur de la

voie de transduction des signaux JNK et/ou un inhibiteur de la voie de transduction des signaux

MAPK/ERK et/ou un stimulateur de la voie de transduction des signaux p38.

L17 ANSWER 6 OF 9 PCTFULL COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER: 1999020755 PCTFULL ED 20020515

TITLE (ENGLISH):

NOVEL CYTOKINE RECEPTORS

TITLE (FRENCH): INVENTOR(S):

NOUVEAUX RECEPTEURS DE CYTOKINE

ELSON, Greg;

GAUCHAT, Jean-Francois; KOSCO-VILBOIS, Marie

GLAXO GROUP LIMITED;

ELSON, Greg;

GAUCHAT, Jean-Francois; KOSCO-VILBOIS, Marie

LANGUAGE OF PUBL.:

PATENT ASSIGNEE(S):

English Patent

DOCUMENT TYPE:

PATENT INFORMATION:

NUMBER

KIND DATE

WO 9920755

A2 19990429

DESIGNATED STATES

W:

AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO
RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM
AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
INFO.:
WO 1998-EP6497
A 19981014

APPLICATION INFO.: WO 1998-EP6497 A 19981014 PRIORITY INFO.: GB 1997-9721961.2 19971016

ABEN A novel polypeptide that is believed to be a novel type 1 cytokine receptor has been identified

in both mice and in humans and the corresponding cDNA sequences have been obtained. There is a high

degree of conservation of amino acid between the human and murine polypeptides, indicating that this

receptor is functionally important. Polypeptides within the scope of the present invention may be

useful in treating cancer, obesity and immune or developmental disorders. They may also be useful in screening.

ABFR On a identifie un nouveau polypeptide dont on estime qu'il est un nouveau type de recepteur de

cytokine 1; cette identification s'est faite a la fois chez des souris et chez des humains et l'on a

obtenu les sequences correspondantes d'ADN complementaire. Le degre de conservation d'acide amine

est eleve dans ces polypeptides humains et murins, ce qui indique que ce recepteur est important du

point de vue fonctionnel. Les polypeptides relevant de cette invention peuvent se reveler efficaces

s'agissant de traitement du cancer, de l'obesite ainsi que d'affections immunitaires et de troubles $\frac{1}{2}$

du developpement. Ils se revelent egalement utiles pour des criblages.

L17 ANSWER 7 OF 9 PCTFULL COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER: 1998009524 PCTFULL ED 20020514

TITLE (ENGLISH): METHODS AND COMPOSITIONS FOR LIVER SPECIFIC DELIVERY OF

THERAPEUTIC MOLECULES USING RECOMBINANT AAV VECTORS

TITLE (FRENCH): PROCEDES ET COMPOSITIONS DESTINES A UNE ADMINISTRATION

SPECIFIQUE DANS LE FOIE DE MOLECULES THERAPEUTIQUES EN

UTILISANT DES VECTEURS RECOMBINANTS AAV

INVENTOR(S): SRIVASTAVA, Aron;

PONNAZHAGAN, Selvarangan;

CHLOEMER, Robert, H.;

WANG, Xu-Shan; YODER, Mervin, C.; ZHOU, Shang-Zhen; ESCOBEDO, Jaime; DWARKI, Varavani

CHIRON CORPORATION; INDIANA UNIVERSITY

LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

PATENT ASSIGNEE(S):

NUMBER KIND DATE

WO 9809524 A1 19980312

DESIGNATED STATES

W: CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT

SE

APPLICATION INFO.: WO 1997-US15453 A 19970902 PRIORITY INFO.: US 1996-60/025,616 19960906 US 1996-60/025,649 19960911

ABEN Provided are methods for selectively expressing therapeutic molecules,

such as secretory proteins, antisense molecules and ribozymes, in the liver. The methods find use in treating hepatic diseases or conditions. The methods also find use in treating any disease or condition in which systemic administration of the therapeutic substance, for example, a secretory protein, is desired. The methods involve administering to a mammalian patient having a need for liver expression of a therapeutic molecule an AAV vector containing a therapeutically effective amount of the therapeutic molecule. Also provided are novel vectors employable in these methods. ABFR L'invention concerne des procedes d'expression selective dans le foie de molecules therapeutiques, telles que des proteines secretrices, des molecules antisens et des ribozymes. On peut utiliser ces procedes dans le traitement d'affections ou de troubles hepatiques. On peut egalement utiliser ces procedes dans le traitement de toute affection ou trouble pour lequel on souhaite une administration systemique de la substance therapeutique, par exemple une proteine secretrice. Les procedes comprennent l'administration a un patient mammifere presentant un besoin d'expression hepatique d'une molecule therapeutique, d'un vecteur AAV contenant une quantite substantielle, du point de vue therapeutique, de la molecule therapeutique. L'invention concerne egalement de nouveaux vecteurs utilisables dans ces procedes. ANSWER 8 OF 9 PCTFULL COPYRIGHT 2004 Univentio on STN ACCESSION NUMBER: 1997046249 PCTFULL ED 20020514 TITLE (ENGLISH): DIAGNOSTIC AND THERAPEUTIC METHODS RELATED TO REGULATING ENERGY MOBILIZATION WITH OB PROTEIN AND OB ANTIBODIES TITLE (FRENCH): PROCEDES DIAGNOSTIQUES ET THERAPEUTIQUES LIES A LA REGULATION DE MOBILISATION D'ENERGIE, PAR PROTEINE OB ET ANTICORPS OB FENG, Lili; INVENTOR (S): CHEN, Sizhong; XIA, Yiyang PATENT ASSIGNEE(S): THE SCRIPPS RESEARCH INSTITUTE; FENG, Lili; CHEN, Sizhong; XIA, Yiyang LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE ______ WO 9746249 A1 19971211 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI

DESIGNATED STATES

SK TJ TM TR TT UA UG US UZ VN YU GH KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.: WO 1997-US9684 A 19970604 PRIORITY INFO.: US 1996-60/018,972 19960604

ABEN Compositions comprising OB-R agonists and methods of treatment for

L17

OB protein, also known as leptin. Also provided are methods and compositions for the treatment of obesity and OB resistance. Assay methods and kits relating to these conditions are also included. ABFR L'invention concerne des compositions a base d'agonistes pour recepteurs OB (OB-R) et des procedes de traitement pour certains etats comme le syndrome de reaction inflammatoire generale. La proteine humaine OB recombinee, egalement appelee leptine, est un ligand agoniste approprie pour OB-R. On decrit aussi des procedes et des compositions pour le traitement de l'obesite et la resistance propre aux OB, ainsi que des epreuves et des necessaires a essai pour les etats consideres. T₁17 ANSWER 9 OF 9 PCTFULL COPYRIGHT 2004 Univentio on STN ACCESSION NUMBER: 1997019952 PCTFULL ED 20020514 TITLE (ENGLISH): THE OB RECEPTOR AND METHODS OF DIAGNOSING AND TREATING WEIGHT TITLE (FRENCH): RECEPTEUR OB ET PROCEDES DE DIAGNOSTIC ET DE TRAITEMENT DES DEREGLEMENTS DE LA MASSE CORPORELLE INVENTOR (S): TARTAGLIA, Louis, A.; TEPPER, Robert, I.; CULPEPPER, Janice, A.; WHITE, David, W. PATENT ASSIGNEE(S): MILLENNIUM PHARMACEUTICALS, INC.; TARTAGLIA, Louis, A.; TEPPER, Robert, I.; CULPEPPER, Janice, A.; WHITE, David, W. LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE WO 9719952 A1 19970605 DESIGNATED STATES AL AM AT AU AZ BB BG BR BY CA CH CN CU CZ DE DK EE ES W: FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG APPLICATION INFO.: WO 1996-US19128 A 19961127 PRIORITY INFO.: US 1995-8/562,663 19951127 US 1995-8/566,622 19951204 US 1995-8/569,485 19951208 US 1995-8/570,142 19951211 US 1995-8/583,153 19951228 US 1996-8/599,455 19960122 US 1996-8/638,524 19960426 US 1996-8/708,123 19960903 ABEN The present invention relates to the discovery, identification and characterization of nucleotides that encode Ob receptor (ObR), a receptor protein that participates in mammalian body weight regulation. The invention encompasses obR nucleotides, host cell expression systems, ObR

inflammatory response syndrome are provided. One suitable OB-R agonist

conditions such as systemic

ligand is recombinant human

proteins, fusion proteins, polypeptides and peptides, antibodies to the receptor, transgenic animals that express an obR transgene, or recombinant knock-out animals that do not express the ObR, antagonists and agonists of the receptor, and other compounds that modulate obR gene expression or ObR activity that can be used for diagnosis, drug screening, clinical trial monitoring, and/or the treatment of body weight disorders, including but not limited to obesity, cachexia and anorexia. Cette invention concerne la decouverte, l'identification et la ABFR caracterisation de nucleotides qui codent le recepteur Ob (ObR), une proteine de recepteur qui participe a la regulation de la masse corporelle chez les mammiferes. Cette invention concerne des nucleotides obR, des systemes d'expression de cellule hote, des proteines ObR, des proteines de fusion, des polypeptides et des peptides, des anticorps diriges contre le recepteur, des animaux transgeniques qui expriment un transgene obR ou des animaux morts produits par recombinaison qui n'expriment pas ObR, des antagonistes et des agonistes du recepteur, et d'autres composes qui modulent l'expression du gene obR ou l'activite de ObR et qu'on peut utiliser pour le diagnostic, la recherche de medicaments, la surveillance des essais cliniques et/ou le traitement des dereglements de la masse corporelle incluant entre autres l'obesite, la cachexie et l'anorexie. => d his (FILE 'HOME' ENTERED AT 16:29:02 ON 23 AUG 2004) FILE 'MEDLINE, SCISEARCH, CAPLUS, BIOSIS, USPATFULL, PCTFULL' ENTERED AT 16:29:49 ON 23 AUG 2004 L1161020 S ((INTERLEUKIN OR IL)(W)6) OR IL6 L21168469 S OBESITY OR OBESE OR FAT OR (BODY(W) (MAASS OR WEIGHT)) L322254 S (KNOCK(W)OUT(W) (MICE OR MOUSE)) OR (NULL(W) (MICE OR MOUSE)) 10196794 S TREAT? OR ADMINISTER? T.4 L52018 S L1(S)L2 299 S L1(S)L3 L6 L7 25249 S L1(S)L4 L834 S L5 AND L6 AND L7 L934 DUP REM L8 (0 DUPLICATES REMOVED) L10 18483 S LEPTIN(S)L2 332 S L10 AND L5 L11102 S L1(P) (SERUM(W) TRIGLYCERIDE?) L12L13 2 S L11 AND L12 2 DUP REM L13 (0 DUPLICATES REMOVED) L14

L15

L16

L17

81 S L11 AND L7

9 S L16 AND PY<=2000

73 DUP REM L15 (8 DUPLICATES REMOVED)

2 2702 (treat\$ or administer\$ or dose) with (((interleukin or iI) adj "6") DERWENT USPAT; US-PGPUB; EPO; DERWENT	3	2702 109975 322	(treat\$ or administer\$ or dose) with (((interleukin or iI) adj "6") or iI6) (body adj (fat or mass or weight)) or obesity or obese (((interleukin or iI) adj "6") or iI6) same ((body adj (fat or	USPAT; US-PGPUB; EPO; DERWENT USPAT; US-PGPUB; EPO; DERWENT USPAT; US-PGPUB; EPO; DERWENT USPAT; US-PGPUB;	2004/08/23 16:49 2004/08/23 16:49 2004/08/23 16:50 2004/08/23 16:50
2 2702 2702 (treat\$ or administer\$ or dose) with (((interleukin or ii) adj "6") DERWENT USPAT, US	3	109975 322	or il6) (body adj (fat or mass or weight)) or obesity or obese (((interleukin or il) adj "6") or il6) same ((body adj (fat or	EPO; DERWENT USPAT; US-PGPUB; EPO; DERWENT USPAT; US-PGPUB; EPO; DERWENT USPAT; US-PGPUB;	2004/08/23 16:49
2	3	109975 322	or il6) (body adj (fat or mass or weight)) or obesity or obese (((interleukin or il) adj "6") or il6) same ((body adj (fat or	EPO; DERWENT USPAT; US-PGPUB; EPO; DERWENT USPAT; US-PGPUB; EPO; DERWENT USPAT; US-PGPUB;	2004/08/23 16:50
2 2702 (treat\$ or administer\$ or dose) with (((interleukin or iI) adj "6") or iI6) DERWENT US-PGPUB; EPO; DERWENT US-PGPUB; DERWENT U	3	109975 322	or il6) (body adj (fat or mass or weight)) or obesity or obese (((interleukin or il) adj "6") or il6) same ((body adj (fat or	DERWENT USPAT; US-PGPUB; EPO; DERWENT USPAT; US-PGPUB; EPO; DERWENT USPAT; US-PGPUB;	2004/08/23 16:50
2	3	109975 322	or il6) (body adj (fat or mass or weight)) or obesity or obese (((interleukin or il) adj "6") or il6) same ((body adj (fat or	USPAT; US-PGPUB; EPO; DERWENT USPAT; US-PGPUB; EPO; DERWENT USPAT; US-PGPUB;	2004/08/23 16:50
109975		322	or il6) (body adj (fat or mass or weight)) or obesity or obese (((interleukin or il) adj "6") or il6) same ((body adj (fat or	US-PGPUB; EPO; DERWENT USPAT; US-PGPUB; EPO; DERWENT USPAT; US-PGPUB;	2004/08/23 16:50
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3		322	(((interleukin or il) adj "6") or il6) same ((body adj (fat or	USPAT; US-PGPUB; EPO; DERWENT USPAT; US-PGPUB;	
4 322 ((((interleukin or iI) adj "6") or iI6) same ((body adj (fat or mass or weight)) or obesity or obese) 5 165 ((treat\$ or administer\$ or dose) with (((interleukin or iI) adj "6") or iI6) same ((body adj (fat or mass or weight)) or obesity or obese)) 6 265 (((interleukin or iI) adj "6") or iI6) with agonist 7 42 ((((interleukin or iI) adj "6") or iI6) with agonist 8 24584 (diabetes adj type) or (abdominal adj obesity) or (obesity) or (metabolic adj syndrome) 9 29 (((treat\$ or administer\$ or dose) with (((interleukin or iI) adj "6") or iI6) with agonist) same ((treat\$ or administer\$ or dose) with (((interleukin or iI) adj "6") or iI6)) 10 8 ((((interleukin or iI) adj "6") or iI6) with agonist) and (((treat\$ or administer\$ or dose) with (((interleukin or iI) adj "6") or iI6)) 10 8 ((((interleukin or iI) adj "6") or iI6) with agonist) and (((treat\$ or administer\$ or dose) with (((interleukin or iI) adj "6") or iI6)) 10 8 ((((interleukin or iI) adj "6") or iI6) with agonist) and (((treat\$ or administer\$ or dose) with (((interleukin or iI) adj "6") or iI6)) 11 9 (((interleukin or iI) adj "6") or iI6) adj agonist 12 (((interleukin or iI) adj "6") or iI6) adj agonist 13 (((interleukin or iI) adj "6") or iI6) ame ((diabetes adj type) or (abdominal adj obesity) or (obesity) or (metabolic adj syndrome))) 14 (((interleukin or iI) adj "6") or iI6) adj agonist 15 (((interleukin or iI) adj "6") or iI6) adj agonist 16 (((interleukin or iI) adj "6") or iI6) adj agonist 17 (((interleukin or iI) adj "6") or iI6) same ((diabetes adj type) or (abdominal adj obesity) or (abdominal adj obesi	4			US-PGPUB; EPO; DERWENT USPAT; US-PGPUB;	
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322 ((((interleukin or il) adj "6") or il6) same ((body adj (fat or mass or weight)) or obesity or obese) 5	4			DERWENT USPAT; US-PGPUB;	2004/08/23 16:50
4 322 ((((interleukin or iI) adj "6") or iI6) same ((body adj (fat or mass or weight)) or obesity or obese) USPAT; USPGPUB; EPO; DERWENT USPAT; USPAT; USPGPUB; EPO; DERWENT USPAT;	4			USPAT; US-PGPUB;	2004/08/23 16:50
mass or weight)) or obesity or obese mass or weight)) or obesity or obese mass or weight)) or obesity or obese mass or weight) or obesity or obese c		165		US-PGPUB;	200 1/00/20 10:00
165 ((treat\$ or administer\$ or dose) with (((interleukin or ii) adj "6") or ii6) ame ((body adj (fat or mass or weight)) or obesity or obese)) ((interleukin or ii) adj "6") or ii6) with agonist ((interleukin or ii) adj "6") or ii6) with agonist ((interleukin or ii) adj "6") or ii6) with agonist ((interleukin or ii) adj "6") or ii6) with agonist ((interleukin or ii) adj "6") or ii6) with agonist ((interleukin or ii) adj "6") or ii6) with agonist ((interleukin or ii) adj "6") or ii6) ((interleukin or ii		165	<i>3 </i>		1
165		165		I FP().	
165		165		1 '	
10 10 10 10 10 10 10 10	5		((treat\$ or administer\$ or dose) with (((interleukin or il) adi		2004/08/23 16:52
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VS-PGPUB; EPO; DERWENT USPAT; US-PGPUB; EPO; DERWENT US-PGPUB; EPO; DERW	6	265	(((interleukin or il) adi "6") or il6) with agonist		2004/08/23 16:52
42 ((((interleukin or iI) adj "6") or iI6) with agonist) same ((treat\$ DERWENT USPAT; US-PGPUB; EPO; DERWENT USPAT; US-PGPUB;			(((· · · · · · · · · · · · · · · · · ·		2004/00/23 10.32
42 ((((interleukin or il) adj "6") or il6) with agonist) same ((treat\$ or administer\$ or dose) with (((interleukin or il) adj "6") or il6)) 24584 (diabetes adj type) or (abdominal adj obesity) or (obesity) or (metabolic adj syndrome) 29 ((treat\$ or administer\$ or dose) with (((interleukin or il) adj "6") or il6)) same ((diabetes adj type) or (abdominal adj obesity) or (obesity)		ĺ		· ·	
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or administer\$ or dose) with (((interleukin or iI) adj "6") or iI6)) US-PGPUB; EPO; DERWENT USPAT; US-PGPUB; Same ((diabetes adj type) or (abdominal adj obesity) or or administer\$ or dose) with (((interleukin or iI) adj "6") or iI6) with agonist) and (((treat\$ or administer\$ or dose) with (((interleukin or iI) adj "6") or iI6)) adj "6") or iI6) with agonist) or (obesity) or (metabolic adj syndrome))) (((interleukin or iI) adj "6") or iI6) adj agonist 12	7	42	((((interleukin or il) adi "6") or il6) with agonist) same ((treat\$		2004/08/23 17:05
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9 29 ((treat\$ or administer\$ or dose) with (((interleukin or iI) adj "6") or iI6)) same ((diabetes adj type) or (abdominal adj obesity) or (obesity) or (metabolic adj syndrome)) 10 8 ((((interleukin or iI) adj "6") or iI6) with agonist) and (((treat\$ or administer\$ or dose) with (((interleukin or iI) adj "6") or iI6)) same ((diabetes adj type) or (abdominal adj obesity) or (obesity) or (metabolic adj syndrome))) 11 9 (((interleukin or iI) adj "6") or iI6) adj agonist 12 151 (((interleukin or iI) adj "6") or iI6) same ((diabetes adj type) or (abdominal adj obesity) or (metabolic adj type) or (abdominal adj obesity)			(metabolic adi syndrome)		2004/00/23 17.00
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10 8 ((((interleukin or il) adj "6") or il6) with agonist) and (((treat\$ USPAT; USPGPUB; EPO; DERWENT ((diabetes adj type) or (abdominal adj obesity) or il6)) same ((diabetes adj type) or (abdominal adj obesity) or (obesity) or (metabolic adj syndrome))) 11 9 (((interleukin or il) adj "6") or il6) adj agonist 12 151 (((interleukin or il) adj "6") or il6) same ((diabetes adj type) or (abdominal adj obesity) or (metabolic adj syndrome))) 12 151 (((interleukin or il) adj "6") or il6) same ((diabetes adj type) or (abdominal adj obesity) or (obesity) or (metabolic adj uSPAT; US-PGPUB;	9	29	((treat\$ or administer\$ or dose) with (((interleukin or il) adi		2004/08/23 17:15
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10 8 ((((interleukin or il) adj "6") or il6) with agonist) and (((treat\$ USPAT; Or administer\$ or dose) with (((interleukin or il) adj "6") or il6)) same ((diabetes adj type) or (abdominal adj obesity) or (obesity) or (metabolic adj syndrome))) 11 9 (((interleukin or il) adj "6") or il6) adj agonist 12 151 (((interleukin or il) adj "6") or il6) same ((diabetes adj type) or (abdominal adj obesity) or (obesity) or (metabolic adj uSPAT; US-PGPUB; US-PGPUB			obesity) or (obesity) or (metabolic adi syndrome))		
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or administer\$ or dose) with (((interleukin or iI) adj "6") or iI6)) same ((diabetes adj type) or (abdominal adj obesity) or (obesity) or (metabolic adj syndrome))) (((interleukin or iI) adj "6") or iI6) adj agonist 12 151 (((interleukin or iI) adj "6") or iI6) same ((diabetes adj type) or (abdominal adj obesity) or (obesity) or (metabolic adj US-PGPUB; EPO; DERWENT US-PGPUB; EVO; DERWENT US-PGPUB; US-PGPUB; US-PGPUB; US-PGPUB; US-PGPUB;	10	8	((((interleukin or il) adj "6") or il6) with adonist) and (((treat\$		2004/08/23 17:09
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(obesity) or (metabolic adj syndrome))) (((interleukin or il) adj "6") or il6) adj agonist USPAT; US-PGPUB; EPO; DERWENT US-PGPUB; EPO; DERWENT US-PGPUB; EPO; DERWENT US-PGPUB; US-PGPUB; US-PGPUB; US-PGPUB; US-PGPUB; US-PGPUB;			same ((diabetes adj type) or (abdominal adj obesity) or		
9 (((interleukin or il) adj "6") or il6) adj agonist USPAT; US-PGPUB; EPO; DERWENT USPAT; USP		l	(obesity) or (metabolic adj syndrome)))		
12 US-PGPUB; EPO; DERWENT USPAT; US-PGPUB; (((interleukin or il) adj "6") or il6) same ((diabetes adj type) or (abdominal adj obesity) or (obesity) or (metabolic adj US-PGPUB;	11	9			2004/08/23 17:16
12 151 (((interleukin or il) adj "6") or il6) same ((diabetes adj type) or (abdominal adj obesity) or (obesity) or (metabolic adj US-PGPUB;			, , , ,		200 1100/20 11.10
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(abdominal adj obesity) or (obesity) or (metabolic adj US-PGPUB;			(abdominal adj obesity) or (obesity) or (metabolic adi		
syndrome))) and ((treat\$ or administer\$ or dose) with EPO:			syndrome))) and ((treat\$ or administer\$ or dose) with		
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